

Remarks

Status of the Claims

Claims 1, 2, 4-8, 11-19, 24, 25, 29, 34-37 and 46-55 are pending in the present application. Applicants have amended claims 1, 2, 4, 7, 8, 11, 24, 29, 36, 46, 49-51, 53 and 54. Applicants have canceled claims 25, 34, 35, 37 and 48, and have added new claims 56-59. Upon entry of these amendments, claims 1, 2, 4-8, 11-19, 24, 29, 36, 46, 47, and 49-59 will be pending in the application.

Support for claims 1, 2, 4, 29, 36, 46, 49, 53, 57 and 58 is found in the specification at least, for example, at page 9, lines 1-23; in Example 1; and in original claim 20. Support for claim 11 is found at least, for example, in claim 7. Support for claim 50 is found at least, for example, at page 10, lines 14-16. Support for claim 51 is found at least, for example, at page 9, lines 1-23; in Example 1; in original claim 20; and at page 10, lines 10-18. Support for claims 56 and 59 is found at least, for example, at page 9, lines 1-23; at page 10, lines 14-16; in Example 1; and in original claim 20. Claims 7, 8, 24 and 54 are amended to remove unnecessary words or to change dependencies.

Applicants submit that the amendments introduce no new matter into the application.

Claim Rejections under 35 U.S.C. § 112

Claims 1, 2, 4-8, 11-19, 24, 25, 29, 34-37 and 46-55 stand rejected under 35 U.S.C. § 112, first and second paragraphs. Applicants have canceled claims 25, 34, 35, 37 and 48. Applicants respectfully traverse the rejection as applied to the pending claims.

The Office action states that the phrase “alteration to a hydrophobic or non-polar amino acid,” as recited in claims 1, 29, 49 and 51 can be interpreted in more than one way, and that one interpretation allegedly introduces new matter (see Office action, pp. 2 and 3). Applicants have amended claims 1, 29, 49 and 51 to clarify the claimed subject matter. Applicants submit that claims 1, 29, 49 and 51, as amended, fully comport with 35 U.S.C. § 112, first and second paragraphs.

Claim 11 has been amended to recite “said part of an Ig heavy chain,” and claim 29 has been amended to clarify that the amino acid alteration increases the circulating half-life of the fusion protein. Claim 53 has been amended to clarify that the C-terminal lysine is altered to a nonpolar or hydrophobic amino acid. Applicants submit that claims 11, 29 and 53, as amended, comport fully with 35 U.S.C. § 112, first and second paragraphs.

Accordingly, Applicants request that the rejections under 35 U.S.C. § 112, first and second paragraphs be reconsidered and withdrawn.

Claim Rejection under 35 U.S.C. § 103

Claims 1, 2, 4-8, 13-19, 24, 29, 34, 36, 37, 46 and 48-52 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over International Publication No. WO 99/43713 to Gillies *et al.* (“Gillies”) in view of U.S. Patent Nos. 5,908,626 or 5,723,125 to Chang *et al.* (“Chang”). Applicants have canceled claims 34, 37 and 48. Applicants respectfully traverse the rejection as applied to the pending claims.

Applicants have amended claim 1 to recite an antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the C-terminal non-Ig protein comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids of the N-terminus of the C-terminal non-Ig protein. Gillies and Chang fail to teach or suggest a fusion protein with a C-terminal non-Ig protein comprising an amino acid substitution within 10 amino acids of the N-terminus of the C-terminal non-Ig protein. Accordingly, Applicants submit that Gillies and Chang cannot render obvious claim 1 or any claim (*e.g.*, 2, 5, 13, 24, 29, 46 and 47) depending from claim 1.

Applicants have amended claim 49 to recite an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the Ig chain comprising an IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE constant domain and an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids from the C-terminus of the Ig chain. Gillies and Chang fail to teach or suggest a fusion protein with an Ig chain comprising an IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE constant domain and an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids from the C-terminus of the Ig chain.

Applicants thus submit that Gillies and Chang cannot render obvious claim 49, or any claim (*e.g.*, 2, 4, 7, 8, 24, 46 and 50) depending from claim 49.

Applicants have amended claim 51 to recite an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the Ig chain comprising at least one of a CH2 and CH3 domain and an amino acid sequence that is non-natural within 10 amino acids from its C-terminus, the non-natural amino acid sequence comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid. Gilles and Chang fail to teach or suggest a fusion protein with an Ig chain comprising an amino acid sequence that is non-natural within 10 amino acids from its C-terminus, wherein the non-natural amino acid sequence comprises an amino acid substitution introducing a hydrophobic or non-polar amino acid. Applicants thus submit that Gillies and Chang cannot render obvious claim 51, or any claim (*e.g.*, 2, 4, 7, 8, 24, 46 or 52) depending from claim 51.

Applicants have added new claim 56, which recites an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the Ig chain comprising at least one of a CH2 and a CH3 domain, and the C-terminal non-Ig protein comprising an amino acid alteration within 10 amino acids of the N-terminus of the C-terminal non-Ig protein, the alteration introducing an amino acid selected from the group consisting of Leu and Trp. Gillies and Chang fail to teach or suggest a fusion protein with an amino acid alteration within 10 amino acids of the N-terminus of a C-terminal non-Ig protein, wherein the alteration introduces an amino acid selected from the group consisting of Leu and Trp. Applicants therefore submit that Gillies and Chang cannot render obvious claim 56.

Applicants have added new claim 57, which recites an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the Ig chain comprising an amino acid substitution within 10 amino acids from the C-terminus, the substitution replacing a charged amino acid with a hydrophobic or non-polar amino acid. Gillies and Chang fail to teach or suggest a fusion protein with an Ig chain comprising an amino acid substitution within 10 amino acids from the C-terminus, wherein the substitution replaces a charged amino acid with

a hydrophobic or non-polar amino acid. Accordingly, Applicants submit that Gillies and Chang cannot render obvious claim 57, or claim 46, which depends therefrom.

Applicants have added new claim 58, which recites an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the N-terminal Ig chain comprising an amino acid substitution within 10 amino acids from the C-terminus of the Ig chain, the substitution introducing a hydrophobic or non-polar amino acid selected from the group consisting of Ala, Gly and Trp. Gilles and Chang fail to teach or suggest a fusion protein with an amino acid substitution within 10 amino acids from the C-terminus of an Ig chain, wherein the substitution introduces an amino acid selected from the group consisting of Ala, Gly and Trp. Applicants thus submit that Gillies and Chang cannot render obvious claim 58.

Applicants have added new claim 59, which recites an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the N-terminal Ig protein comprising a CH3 domain, wherein the CH3 domain comprises a deletion of a charged amino acid within 10 amino acids of the C-terminus of the CH3 domain. Chang and Gillies fail to teach or suggest a fusion protein with a CH3 domain comprising a deletion of a charged amino acid within 10 amino acids of its C-terminus. As such, Applicants submit that Gillies and Chang cannot render obvious claim 59.

Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim Rejections under 35 U.S.C. § 102

Fell et al., (1991), The Journal of Immunology, 146(7):2446-2452 ("Fell")

Claims 1, 2, 4-7, 11-14, 16, 24, 25, 29, 34-37 and 46-52 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Fell. Applicants have canceled claims 25, 34, 35, 37 and 48. Applicants respectfully traverse the rejection as applied to the pending claims.

Applicants have amended claim 1 to recite an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the C-terminal non-Ig protein comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids of the N-terminus of the C-terminal non-Ig protein. Fell fails to teach or suggest

a fusion protein with a non-Ig protein comprising an amino acid substitution within 10 amino acids of the N-terminus of the non-Ig protein. Accordingly, Applicants submit that Fell cannot anticipate claim 1 or any claim (*e.g.*, 2, 5, 13, 24, 29, 46 and 47) depending from claim 1.

Applicants have amended claim 49 to recite an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the Ig chain comprising an IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE constant domain and an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids from the C-terminus of the Ig chain. Fell fails to teach or suggest a fusion protein with an IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE constant domain. Applicants thus submit that Fell cannot anticipate claim 49 or any claim (*e.g.*, 2, 4, 7, 8, 24, 46 and 50) depending from claim 49.

Applicants have amended claim 51 to recite an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the Ig chain comprising at least one of a CH2 and CH3 domain, and an amino acid sequence that is non-natural within 10 amino acids from its C-terminus, the non-natural amino acid sequence comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid. Fell fails to teach or suggest a fusion protein with an Ig chain comprising at least one of a CH2 and a CH3 domain. Applicants thus submit that Fell cannot anticipate claim 51, or any claim (*e.g.*, 2, 4, 7, 8, 24, 46 or 52) depending from claim 51.

Applicants have added new claim 56, which recites an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the Ig chain comprising at least one of a CH2 and a CH3 domain and the C-terminal non-Ig protein comprising an amino acid alteration within 10 amino acids of the N-terminus of the C-terminal non-Ig protein, the alteration introducing an amino acid selected from the group consisting of Leu and Trp. Fell fails to teach or suggest a fusion protein with an Ig chain comprising at least one of a CH2 and a CH3 domain. Applicants therefore submit that Fell cannot anticipate claim 56.

Applicants have added new claim 57, which recites an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the Ig chain comprising an amino acid substitution within 10 amino acids from the C-terminus, the substitution replacing

a charged amino acid with a hydrophobic or non-polar amino acid. Fell fails to teach or suggest a fusion protein with an Ig chain comprising an amino acid substitution that replaces a charged amino acid. Accordingly, Applicants submit that Fell cannot anticipate claim 57.

Applicants have added new claim 58, which recites an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the N-terminal Ig chain comprising an amino acid substitution within 10 amino acids from the C-terminus of the Ig chain, the substitution introducing an amino acid selected from the group consisting of Ala, Gly and Trp. Fell fails to teach or suggest a fusion protein with an amino acid substitution within an Ig chain introducing an amino acid selected from the group consisting of Ala, Gly and Trp. Applicants therefore submit that Fell cannot anticipate claim 58.

Applicants have added new claim 59, which recites an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the N-terminal Ig protein comprising a CH3 domain, wherein the CH3 domain comprises a deletion of a charged amino acid within 10 amino acids of the C-terminus of the CH3 domain. Fell fails to teach or suggest a fusion protein with an Ig protein comprising a CH3 domain. As such, Applicants submit that Fell cannot anticipate claim 59.

International Publication Number WO 98/28427 to Mann *et al.* ("Mann")

Claims 1, 2, 4-8, 11, 12, 24, 34, 36, 37 and 46-52 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Mann. Applicants have canceled claims 34, 37 and 48. Applicants respectfully traverse the rejection as applied to the pending claims.

Applicants have amended claim 1 to recite an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the C-terminal non-Ig protein comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids of the N-terminus of the C-terminal non-Ig protein. Mann fails to teach or suggest a fusion protein with a non-Ig protein comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids of the N-terminus of the non-Ig protein. Accordingly, Applicants submit that Mann cannot anticipate claim 1 or any claim (*e.g.*, 2, 5, 13, 24, 29, 46 and 47) depending from claim 1.

Amended claims 49 and 51 and new claims 57 and 58 relate to an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the Ig chain comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids from the C-terminus of the Ig chain. Mann fails to teach or suggest a fusion protein with an Ig chain comprising an amino acid substitution introducing a hydrophobic or non-polar amino acid within 10 amino acids from the C-terminus of the Ig chain. Applicants thus submit that Mann cannot anticipate claim 49, 51, 57 or 58, or any claim (*e.g.*, 2, 4, 7, 8, 24, 46, 50 and 52) depending from them.

Applicants have added new claim 56, which recites an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the Ig chain comprising at least one of a CH2 and a CH3 domain and the C-terminal non-Ig protein comprising an amino acid alteration within 10 amino acids of the N-terminus of the C-terminal non-Ig protein, the alteration introducing an amino acid selected from the group consisting of Leu and Trp. Mann fails to teach or suggest a fusion protein with an amino acid alteration within 10 amino acids of the N-terminus of a C-terminal non-Ig protein, wherein the alteration introduces an amino acid selected from the group consisting of Leu and Trp. Applicants therefore submit that Mann cannot anticipate claim 56.

Applicants have added new claim 59, which recites an antibody-based fusion protein comprising an N-terminal Ig chain linked to a C-terminal non-Ig protein, the N-terminal Ig protein comprising a CH3 domain, wherein the CH3 domain comprises a deletion of a charged amino acid within 10 amino acids of the C-terminus of the CH3 domain. Mann fails to teach or suggest a fusion protein with an Ig protein comprising a CH3 domain, wherein the CH3 domain comprises a deletion of a charged amino acid within 10 amino acids of its C-terminus. As such, Applicants submit that Mann cannot anticipate claim 59.

Applicants respectfully request reconsideration and withdrawal of the rejection.

Conclusion

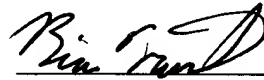
Claims 1, 2, 4-8, 11-19, 24, 29, 36, 46, 47 and 49-59 are pending and believed to be in condition for allowance. Examiner Saunders is invited to telephone the undersigned attorney to discuss any remaining issues.

Respectfully submitted,

Date: June 9, 2004
Reg. No. 48,645

Tel. No.: (617) 248-7697
Fax No.: (617) 248-7970

3070374



Brian Fairchild, Ph.D.
Attorney for Applicant(s)
Testa, Hurwitz, & Thibeault, LLP
High Street Tower
125 High Street
Boston, Massachusetts 02110